Serum Lipoprotein and Cholesterol Concentrations
Comparison of Rural Costa Rican, Guatemalan, and United States Populations

By Nevin S. Schimshaw, Ph.D., M.D., Martha Trulson, D.Sc., Carlos Tejada, M.D., D. Mark Hegsted, Ph.D., and Fredrick J. Stare, M.D.

A previous study indicated that Guatemalan Indians, both male and female, tended to maintain low levels of serum cholesterol throughout adulthood but that beta-lipoprotein fractions increased with age, as is usually the case in populations in the United States. To investigate whether race was of importance in this unexpected dissociation between these lipid fractions, a similar study was done with a rural group in Costa Rica, which was comparable in the diet consumed and in many other environmental factors, but of pure European origin. At all ages the cholesterol values were slightly higher but the same type of dissociation was observed.

In a previous report Mann, Munoz, and Schimshaw demonstrated that rural Guatemalans, subsisting on a diet low in both animal protein and calories from fat, had much lower serum cholesterol values than men and women from business and professional families living in urban areas in either Guatemala or the United States. The rural Guatemalans also showed beta-lipoprotein fractions that were within the same levels for males, and higher levels for females, than upper income populations in urban Guatemala and the United States. This dissociation between serum cholesterol and certain beta-lipoprotein fractions was quite unexpected and contrary to the findings of studies dealing exclusively with United States subjects.

These observations have important implications because autopsy findings indicate that the rural Guatemalan group has a much lower incidence of the complications of atherosclerosis than persons in the United States. Similarly, clinical records show coronary heart disease to be common among business and professional persons in urban areas in both the United States and Guatemala and exceedingly rare among lower income persons residing in rural Guatemala.

These results suggested that environmental differences, among which diet might be the most important determining factor, were responsible for the relative freedom from coronary heart disease and other complications of atherosclerosis of the Guatemalan rural group. This group differed, however, in racial origin: they were known to be predominantly Mayan Indian by their physical appearance, way of life, and the distribution of blood group O, which varied from 80 to 96 per cent, depending on the village studied. In contrast, the United States population is known to have a major blood group frequency of approximately 45 per cent type O, and the upper income Guatemalan population a frequency only slightly higher, which correlates well with the predominantly European origin of this segment of the Guatemalan population. Before accepting environmental variations as responsible for the differences encountered between rural Guatemalans and the other 2 groups it was necessary to be certain that differences in racial origin were not of major significance.

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In the present study comparable information has been obtained on a group of persons living in rural Costa Rica, under conditions similar to those previously studied in rural Guatemala, except that the Costa Rican population is predominantly European by history, physical appearance, and distribution of the major blood groups.

**Material and Methods**

The population of the rural area of Turrialba, Costa Rica, was selected because detailed social, economic, agricultural, dietary, and clinical studies had been carried out on this group. This population is European in origin, with essentially no Negro or Indian admixture. In other respects it resembles the rural Guatemalan Indian population previously studied. The results of the clinical and laboratory examinations showed little difference between the rural Costa Ricans and Guatemalans, except for a greater frequency of hookworm anemia among the former. The rural Guatemalans and United States business and professional groups included for comparison in this paper are those previously studied, plus additional determinations in the latter group. Each subject was examined by a physician, and blood pressure, height, and weight were recorded. For the purposes of the present report, subjects with evidences of acute or chronic disease or a blood pressure exceeding 140/90 were excluded from the tabulations.

**Dietary Data.** Dietary histories were obtained from 140 representative families in the rural area of Turrialba by means of 7-day-diet records. The weekly purchasing pattern of this community facilitated the use of this procedure, which was carried out by a nutritionist familiar with the language, customs, and foods of the people. The nutrient intakes were estimated by means of a food composition table based on the analysis of Central American foods and their dietary allowances modified from those of the National Research Council (U.S.) to conform with local environmental conditions and mean body weights. The collection and calculation of the dietary data on the other 2 groups have been previously described.

**Laboratory Data.** The blood samples were collected in the field and immediately transported to a central laboratory for centrifugation and recovery of the sera. Serum samples, kept at 0 to 5°C, at all times, were placed in labeled tubes for air shipment to Boston. Lipoproteins were measured with the ultracentrifuge by the method of Gofman and co-workers. Although only the β-lipoprotein Sf 12–20 and Sf 35–100 fractions were measured in the previous study, the values for the Sf 0–12, Sf 12–20, and Sf 20–100 were determined in the Costa Rican sample. Our Sf 20–100 measurements are comparable to the “standard” Sf 20–400 values of Delalla and Gofman. Cholesterol was measured by the method of Abell and associates.

**Statistical Data.** The laboratory data for each group were tabulated according to sex and decade of age. The tabulations differed from those presented in the previous paper in that no logarithmic transformations of the measurements were made. The degree of skewness of the distribution was sufficiently slight that this transformation was not considered necessary. The relative weights, (100 × observed weight)/desirable weight were computed for all subjects.

For lack of more suitable reference data, the tables of Desirable Weights* of the Metropolitan Life Insurance Company were used for this calculation. The t test was employed to evaluate the significance of difference between means.

**Results**

A partial summary of the dietary findings in the 3 groups is given in table 1. When compared with the rural Guatemalans previously studied, the diets of the Turrialba rural area population are higher in calories, fat, and cholesterol. The percentage of total calories from fat, although slightly greater than in rural Guatemala, is still less than a third of the percentage given in the United States reports. The amount of protein and fat of animal as compared with vegetable origin, is nearly 3 times greater in the rural Costa Ricans than in the rural Guatemalans, but still much less than for the United States population. It is of interest that the small amount of free fat consumed in Guatemala came from lard, while in Turrialba, some butter and vegetable oil were also used. The cholesterol content of the diets of the 3 groups was estimated and found to be low in the rural Costa Ricans and still lower in the rural Guatemalans.

The levels of cholesterol and lipoproteins of the Sf 12–20 and Sf 20–100 classes for the 3 groups are shown in table 2. The data are grouped according to decade of age and the significance of each comparison is given. When the rural Costa Rican group is compared with the rural Guatemalan group, the serum cholesterol levels tend to be slightly higher, significantly so in 2 age groups for the males and 3 age groups for the females. On the other hand, * Formerly referred to by the Metropolitan Life Insurance Company as “Ideal Weights.”
the $S_1$ 12–20 fraction tended to be lower in rural Costa Ricans, significantly so in 1 age group for each sex. The $S_1$ 20–100 fraction also tended to be somewhat lower in rural Costa Ricans than in the rural Guatemalans. This difference was significant in females, for the decades 30 to 39 and 40 to 49, with a reversal of this trend in the 50 to 59 age group, probably due to the small number of cases in the latter. The direction of the changes tended to put the rural Costa Ricans closer to the values encountered in the urban United States population, but the magnitude of the differences between the rural Costa Rican and rural Guatemalan populations was small.

When the rural Costa Rican was compared
with the urban United States population, the serum cholesterol levels were significantly lower in every decade. However, the trend of the lipoprotein values differed in males and females. Costa Rican males tended to have lower Sf 12–20 and 20–100 values than males of similar age in the United States, although the differences were significant in only about half. On the other hand, a dissociation between cholesterol and lipoprotein was noted in rural Costa Rican women. The Sf 20–100 fraction tended to be significantly higher in the decade 20 to 29. The Sf 12–20 fraction was not significantly different between United States and Costa Rican women.

These trends are shown graphically in figure 1, where the Costa Rican males are intermediate in cholesterol, but tend to be lower in Sf 12–20 and 20–100 levels than the other 2 groups. For the Costa Rican females, the cholesterol and Sf 20–100 levels are seen to be intermediate between the rural Guatemalan and United States groups, but the Sf 12–20 fractions were almost identical in rural Costa Rica and United States.

In the previous study, the levels of the Sf 0–12 lipoprotein fractions were not determined. Table 3 gives the Sf 0–12 concentrations for the rural Costa Ricans and a United States sample done in a different laboratory. The latter is reasonably comparable economically and socially to the United States sample studied in this laboratory. It will be seen that in both sexes and in every decade the Sf 0–12 fractions for the rural Costa Ricans were significantly lower than in the United States population.

The rural Costa Ricans showed the same relative weight as the rural Guatemalans for the earlier decades and this remained unchanged through the 50–59 age group, at which time the relative weight of the rural Guatemalan males showed a significant drop. As shown in table 4, the rural Costa Rican females began at a relative weight below that of the rural Guatemalans, and unlike them, did not show any further decrease in relative weight with increasing age. The rural Costa Ricans showed much lower relative weights than the United States subjects. Analysis of covariance had shown in the previous comparison among rural Guatemalans, urban Guatemalans, and a United States urban population sample that relative weight was of

### Table 3.—Levels of Sf 0–12 Lipoprotein Fractions in Rural Costa Rican and United States Populations

<table>
<thead>
<tr>
<th>Age (yr.)</th>
<th>Group</th>
<th>A compared with C</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Rural Costa Rican</td>
<td>United States*</td>
</tr>
<tr>
<td></td>
<td>N</td>
<td>X</td>
</tr>
<tr>
<td><strong>Males</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20–29</td>
<td>17</td>
<td>197</td>
</tr>
<tr>
<td>30–39</td>
<td>9</td>
<td>239</td>
</tr>
<tr>
<td>40–49</td>
<td>11</td>
<td>247</td>
</tr>
<tr>
<td>50–59</td>
<td>13</td>
<td>220</td>
</tr>
<tr>
<td><strong>Females</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20–29</td>
<td>14</td>
<td>233</td>
</tr>
<tr>
<td>30–39</td>
<td>20</td>
<td>268</td>
</tr>
<tr>
<td>40–49</td>
<td>11</td>
<td>233</td>
</tr>
<tr>
<td>50–59</td>
<td>4</td>
<td>235</td>
</tr>
</tbody>
</table>

* "Standard" Sf 0–12 values; these are slightly lower than "observed" figures as measured on the Costa Ricans.
minor importance in influencing serum lipid levels. This analysis was repeated for the comparison between the rural Costa Rican and United States group, with the same results.

**Discussion**

These observations indicate that the differences previously encountered between the rural Guatemalan population and the urban groups in Guatemala and the United States were not due to racial factors. Furthermore, the differences in serum lipids between the rural Costa Ricans and rural Guatemalans are in general small and not statistically significant. It is of interest that these differences are almost always in the direction of the urban business and professional population in the United States and Guatemala, so that the Costa Ricans can be said to have gone a very small part of the distance toward the type of serum cholesterol and lipoprotein relationships found in the United States.

Table 1 shows that urban Costa Ricans do have slightly more animal protein, slightly more fat, a higher percentage of calories from fat, and more cholesterol in their diets than do the rural Guatemalans. The evidence that dietary cholesterol has no relation to serum cholesterol levels within the range of cholesterol intake under consideration is convincing.17,18 If the difference in serum cholesterol can be attributed to the difference in fat intake, as has been suggested by Keys,19,20 it may be somewhat discouraging from the point of view of prevention to note that differences as small as those existing between these 2 rural populations may have a detectable effect on cholesterol levels. However, assuming serum cholesterol levels correlate with the occurrence of atherosclerosis, the upper limits beyond which the development of atheromata are accelerated are still unknown.

Attention has also been called to the similarity between the predominantly vegetable diet consumed by persons in rural Central America and the "rice diet" regimen for the treatment of essential hypertension. In the latter, Hatch's group21 has reported a lowering of cholesterol values in most cases together with a 9 per cent increase in Sf 12–20 and a 99 per cent rise in Sf 20–100 values. This was associated with an increase in serum neutral fat.

The suggestion has been made that some factor in vegetable protein diets, apart from the major nutrients, might be responsible for a decrease in serum cholesterol levels in persons consuming low-fat diets. Sitosterol has been studied as an example of such a substance.22 However, it has been difficult to conceive of a factor that would be common to low-fat diets in all of the various parts of the world in which low serum cholesterol levels have been encountered. Malmros and Wigand23

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**Table 4.**—Relative Weights by Age and Sex for Rural Costa Ricans, Rural Guatemalans, and United States Subjects

<table>
<thead>
<tr>
<th>Age (yr.)</th>
<th>A Rural Costa Rican</th>
<th>B Rural Guatemalan</th>
<th>A compared with B</th>
<th>C United States</th>
<th>A compared with C</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>X ± SEX</td>
<td>X ± SEX</td>
<td>p</td>
<td>X ± SEX</td>
<td>p</td>
</tr>
<tr>
<td>Males</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20-29</td>
<td>94 ± 1.09</td>
<td>96 ± 2.77</td>
<td>↓</td>
<td>107 ± 1.82</td>
<td>↓</td>
</tr>
<tr>
<td>30-39</td>
<td>90 ± 2.17</td>
<td>96 ± 1.54</td>
<td>↓</td>
<td>107 ± 0.73</td>
<td>↓</td>
</tr>
<tr>
<td>40-49</td>
<td>97 ± 1.62</td>
<td>93 ± 1.89</td>
<td>↑</td>
<td>110 ± 0.45</td>
<td>↓</td>
</tr>
<tr>
<td>50-59</td>
<td>94 ± 1.76</td>
<td>76 ± 2.00</td>
<td>↑</td>
<td>111 ± 0.88</td>
<td>↓</td>
</tr>
<tr>
<td>Females</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20-29</td>
<td>89 ± 4.00</td>
<td>100 ± 3.41</td>
<td>↓</td>
<td>103 ± 2.47</td>
<td>↓</td>
</tr>
<tr>
<td>30-39</td>
<td>91 ± 3.62</td>
<td>93 ± 2.58</td>
<td>↓</td>
<td>107 ± 2.55</td>
<td>↓</td>
</tr>
<tr>
<td>40-49</td>
<td>95 ± 5.05</td>
<td>94 ± 3.92</td>
<td>↑</td>
<td>106 ± 1.55</td>
<td>↓</td>
</tr>
<tr>
<td>50-59</td>
<td>90 ± 4.26</td>
<td>83 ± 3.33</td>
<td>↑</td>
<td>106 ± 2.53</td>
<td>↓</td>
</tr>
</tbody>
</table>
have reported that a fall in serum cholesterol levels accompanied the institution of a diet rich in corn oil in 8 cases of familial hypercholesterolemia. They suggested that these effects might be due to the high essential fatty acid content of corn oil, which contains 57 per cent linoleic acid. This suggestion is supported by the recent observations of Lever and Wadell,23 Kinsell and co-workers,24 Bronte-Stewart,25 and Ahrens.26 However, most of these studies have been on few patients and for short periods of observation. When 1000 calories of an unsaturated vegetable oil (peanut) with 22 per cent linoleic acid were incorporated into the daily diets of 25 men for a period of 4 weeks, we observed a marked drop in cholesterol after 1 or 2 weeks, but by the fourth week the cholesterol values were mostly back at starting levels.27 Thus, the decrease in serum cholesterol reported to follow the generous administration of some oil rich in essential fatty acids may turn out to be only transient when added to the daily diet. Nevertheless, it is of interest that the high-corn diets of Central America, although low in total fat, do at least provide a generous proportion of the essential fatty acid, linoleic acid.

The results again indicate that under the conditions prevailing in Central America, particularly in females, a definite dissociation between the levels of serum lipoprotein and cholesterol occurs. The Guatemalan females can no longer be said to be unique in combining low cholesterol levels with high lipoprotein levels when compared with age-matched North American females, for the Costa Rican females also show this phenomenon in the Sf 20–100 lipoprotein fractions. This discrepancy raises the question as to which fractions in the lipoprotein complex system are involved in the lower levels of cholesterol in the blood stream under the environmental influences prevailing in rural Guatemala and Costa Rica. The cholesterol associated with the various lipoprotein fractions accounts for at least 95 per cent of the total.28 The cholesterol content of the Sf 0–12 fraction alone has been given as approximately 33 per cent.27-30 From the results of the present study it appears that most of the difference in cholesterol levels can be accounted for by the low levels of the Sf 0–12 fraction.

The question may be raised as to whether the rural Costa Rican population is as free from the complications of atherosclerosis as the rural Guatemalan population. Preliminary information being collected by one of us (C. T.) in cooperation with Dr. Rodolfo Cespedes in Costa Rica indicates that the Costa Rican rural population does, in fact, share in this relative immunity from coronary heart disease and other complications of atherosclerosis. If this is true, our data on both the Guatemalans and Costa Ricans, indicating rather minor differences in the serum concentrations of the lipoproteins, Sf 12–100, between these groups and the United States population, but large and significant differences in the Sf 0–12 and cholesterol concentrations between the Costa Rican and United States groups, suggest that these latter 2 fractions may be more intimately related to the development of atherosclerosis than the Sf 12–100 fractions.

There is no doubt that the rural and poor urban populations of Central America consume much less fat than most persons in the United States, derive a far smaller percentage of their total calories from this class of nutrient, and utilize different kinds of fats. Other known differences in the dietary data include the amount of animal protein, the number of calories from refined carbohydrates, and the percentage of crude fiber. In addition, vitamin A and riboflavin intakes are lower and the mineral composition of the diets differ. It is also conceivable that there are other specific factors in the Central American diets that can serve to depress the serum cholesterol. Furthermore, the relative body weights of the rural population are less and they are more active physically. For these reasons, it would be premature to assert which specific environmental factors are the ones responsible for the lower serum cholesterol and freedom from the complications of atherosclerosis of the lower income groups of Central America. Fortunately, the Central American area offers a very favorable opportunity for the continuing investigation of this problem.
SUMMARY

The total cholesterol and major beta-lipoprotein fractions were determined in a group of 99 men and women living in the rural zone of Turrialba, Costa Rica, and subsisting on diets low in fat and animal protein. These measurements were compared with North Americans and rural Guatemalans previously investigated.

At all ages studied the Costa Rican subjects, both male and female, were shown to have mean cholesterol values that were slightly higher than the rural Guatemalans, but much lower than the North Americans. There was little evidence among the Costa Ricans of the tendency for serum cholesterol to increase with age. The \(S_f\) 12–20 and 20–100 levels in the rural Costa Rican males were only slightly lower and in the females were frequently higher than in the North Americans. They tended to be lower, however, than in the rural Guatemalans previously studied. The \(S_f\) 0–12 levels were lower in the rural Costa Ricans than in the North Americans and this difference was sufficient to account for most of the differences in cholesterol levels.

The greater leanness of the rural Costa Rican was shown not to be a significant factor in the lower cholesterol values. Since the rural Costa Rican population was of European origin in contrast to the predominantly Mayan Indian of the rural Guatemalan group previously studied, the similarity of the results in both populations would seem to eliminate racial factors from serious consideration and to confirm the hypothesis that environmental factors, most likely nutritional, are responsible for the differences observed between rural Central Americans and North Americans.

In view of the supposed freedom of Central American rural and low income urban populations from the complications of atherosclerosis it is important that the dietary and other environmental factors be identified that may be responsible for these differences.

Since there are only minor differences in the concentration of the \(S_f\) 12–100 lipoproteins in the United States and Central American groups, but large differences in the serum cholesterol and \(S_f\) 0–12 lipoproteins, the latter 2 fractions may be more closely related to the development of atherosclerosis than the lipoproteins with high flotation rates.

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SUMMARIO IN INTERLINGUA

Le cholesterol total e le major fractiones de lipoproteina beta esseva determinate in un gruppo de 99 homines e feminas habitante le zona rural de Turrialba in Costa Rica e vivente con dietas a basse contento de grassia e proteina animal. Iste mesurationes esseva compaire con datos obtenite in previe investigaciones de nord-americanos e guatemalanos.

Esseva constatate que le costaricanos de ambe sexos e de omne etates representate in le studio habeva valores medie de cholesterol que esseva levemente plus alte que illos del guatemalanos rural sed multi plus basse que illos del nord-americanos. In le costaricanos le tendentia de cholesterol seral de augmentar se con le etate del subjectos esseva pauco evidente. Le nivellos \(S_f\) 12–20 e 20–100 in masculos rural de Costa Rica esseva solmente pauco plus basse que in nord-americanos; in femininas illos esseva frequentemente plus alte. Tamen, iste valores tendeva a esser plus basse que in le previemente studiate guatemalanos rural. Le nivellos \(S_f\) 0–12 esseva plus basse in le costaricanos rural que in le nord-americanos, e iste differentia sufficeva a coperir le plus grande parte del differentias in le nivellos de cholesterol.

Esseva monstrate que le plus grande magressa del costaricano rural non esseva un factor significative in le causation del plus basse valores de cholesterol. Proque le subjectos rural in Costa Rica esseva de origine europee durante que le previemente studiate gruppo de guatemalanos rural esseva predominamente indians mayan, le similaritate del resultatos obtenite in le duo populationes pare
eliminar la posibilidad que factores racial debe ser prendido in consideration e confirma la hipótesis que factores ambiental, probablemente de forma responsables para los cambios observados inter centro-este y nordeste rural.

Visto la observation que le population rural a pequeña ventana en América Central es libre del complicaciones de atherosclerosis, le es importante identifier los factores dietários e alteremente ambiente que es responsable para este diferentías.

Proque il existe solmente minor diferentías in le concentrations del lipoproteinas a Sf 12–100 inter le grupos statounitese e centro-american se le grande diferentías in le cholesterol seral e le lipoproteinas a Sf 0–12, iste ultime fractiones es forsan plus directemente conecté con le dislipidemia de atherosclerosis que le lipoproteinas a Sf 12–100.

REFERENCES


RUPTURE OF THE HEART

I will add another observation: A noble Knight Baronet, Sir Robert Darcie, father to the Son-in-Law of the most learned man, and my very great friend and a famous Physician, Dr. Argent, about the middle of his age, did often complain of an oppressive pain in his breast, especially in the night time, so that sometimes being afraid of collapsion of spirits, sometimes fearing suffocation by a Paroxisme, he led an unquiet and anxious life, using the Counsell of all Physicians, and taking many things in vain; at last the disease prevailing, he becomes cachectick, and Hydropick, and at last oppress in a signal Paroxism, he dyed. In his Corps, in the presence of Dr. Argent, who was President of the College of Physicians, and Dr. Gorge, a rare Divine, and a good Preacher, who was at that time Minister of that Parish, by the hinderance of the passage of the blood out of the left ventricle into the arteries, the wall of the left ventricle it self (which is seen to be thick and strong enough) was broken, and poured forth blood at a wide hole, for it was a hole so big, that it would easily receive one of my fingers.—WILLIAM HARVEY, De Circulatione Sanguinis, 1649.
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